[redacted] [redacted]

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,712	03/30/2001	Gregor Sagner	5443	7485

22829 7590 11/26/2001

ROCHE MOLECULAR SYSTEMS INC
PATENT LAW DEPARTMENT
1145 ATLANTIC AVENUE
ALAMEDA, CA 94501

EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1655	7

DATE MAILED: 11/26/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/823,712	SAgner
Examiner	**Art Unit**
Arun Chakrabarti	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- *If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.*
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- *Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).*
- *Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).*

Status

1) ☒ *Responsive to communication(s) filed on 4/20/01, 5/01/01 and 7/10/01 .*

2a) ☐ *This action is* **FINAL.** 2b) ☒ *This action is non-final.*

3) ☐ *Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

Disposition of Claims

4) ☒ *Claim(s) 1-14 is/are pending in the application.*

4a) *Of the above, claim(s) _____ is/are withdrawn from consideration.*

5) ☐ *Claim(s) _____ is/are allowed.*

6) ☒ *Claim(s) 1-14 is/are rejected.*

7) ☐ *Claim(s) _____ is/are objected to.*

8) ☐ *Claims _____ are subject to restriction and/or election requirement.*

Application Papers

9) ☐ *The specification is objected to by the Examiner.*

10) ☐ *The drawing(s) filed on _____ is/are objected to by the Examiner.*

11) ☐ *The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.*

12) ☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. § 119

13) ☒ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

a) ☐ *All* b) ☐ *Some** c) ☒ *None of:*

1. ☒ *Certified copies of the priority documents have been received.*
2. ☐ *Certified copies of the priority documents have been received in Application No. _____ .*
3. ☐ *Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).*

**See the attached detailed Office action for a list of the certified copies not received.*

14) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

Attachment(s)

15) ☒ *Notice of References Cited (PTO-892)*

16) ☐ *Notice of Draftsperson's Patent Drawing Review (PTO-948)*

17) ☐ *Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____*

18) ☐ *Interview Summary (PTO-413) Paper No(s). _____*

19) ☐ *Notice of Informal Patent Application (PTO-152)*

20) ☐ *Other:*

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 6, 11 and 14, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

Claim 1 recites the limitation "the efficiency" in line 1 and “the cycle number” in line 7. There is insufficient antecedent basis for this limitation in the claim.

Claim 2 recites the limitation "the efficiency" in line 1 and “the cycle number” in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 recites the limitation "the efficiency" in line 1 and “the cycle number” in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 4 recites the limitation "the negative local 1st derivative" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 5 recites the limitation "the reciprocal local 1st derivative" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 recites the limitation "the aid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 7 recites the limitation "the absolute quantification" in line 1 and "the original copy number" in line 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 recites the limitation "the quantification" in line 1 and "the original ratio" in line 11. There is insufficient antecedent basis for this limitation in the claim.

Claim 9 recites the limitation "the relative quantification" in line 1 and "the cycle number" in line 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 10 recites the limitation "the relative quantification" in line 1 and "the cycle number" in line 10. There is insufficient antecedent basis for this limitation in the claim.

Claim 11 recites the limitation "the aid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 12 recites the limitation "the aid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites the limitation "the aid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 14 recites the limitation "the aid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 4 and 5 are also rejected over the recitation of the phrase, "local 1st derivative". It is not clear which locations and which derivative are claimed. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-14 are rejected under 35 U.S.C. 103(a) over Wittwer et al. (PCT International Publication Number WO 97/46707) (December 11, 1997) in view of Brown et al. (U.S. Patent 6,143, 496) (November 7, 2000).

Wittwer et al teach a method for determining the efficiency of the amplification of a target nucleic acid (Abstract) comprising the steps of:

b) the target nucleic acid is amplified under defined reaction conditions and the amplification is measured in real-time (Figures 9A-9G and 11A);

c) a defined signal threshold value is set (Figure 22);

d) determining the cycle number for each dilution at which the signal threshold value is exceeded (Figure 22);

e) determining a non-linear continuously differentiable function of a logarithm of copy number of target nucleic acid used for the amplification as a function of the cycle number at which the signal threshold value is exceeded (Figure 22 and Page 58, lines 1-4 and Page 59, lines 1-15 and Figure 21 D); and

f) calculating the amplification efficiency from the function determined in step e) (Page 59, lines 1-15 and Figure 21 D).

Wittwer et al teach a method, wherein the amplification efficiency of a certain original amount of target nucleic acid is determined as the negative and reciprocal local first derivative of the continuously differentiable function (Page 59, lines 1-15).

Wittwer et al teach a method, wherein the non-linear continuously differentiable function is determined with the aid of polynomial fit of the third degree (Page 59, lines 1-22)

Wittwer et al also teach a method for the absolute quantification of a target nucleic acid in a sample (Abstract and Page 66, lines 16-23)) comprising the steps of:

a) determination of the amplification efficiencies of the target nucleic acid and of an internal or external standard (Figures 22, 45 and 46);

b) amplification of the target nucleic acid contained in the sample and of the standard under the same defined reaction conditions (Figures 22, 45 and 46);

c) measurement of the amplification of the target nucleic acid and standard in real time (Figures 22, 45 and 46);

d) calculation of the original copy number in the sample with the aid of amplification efficiencies determined in step a) (Page 59, lines 1-22).

Wittwer et al. also teach a method, wherein the amplified nucleic acids are detected with the aid of at least one fluorescent-labelled hybridization probe selected from SybreGreen I (Figures 21A-21D).

Wittwer et al. teach correction of copy number with the aid of amplification efficiencies (Figure 59).

Wittwer et al inherently teach calculating the quotients of the function values (copy number) from the target nucleic acid and reference nucleic acid for the sample to be analyzed as well as for the calibrator sample and determination of the ratio of the two quotients as a measure for the original amount of target nucleic acid contained in the sample (Figures 14, 20, 22, 29 and 57 and Page 93, line 12 to page 94, line 13).

Wittwer et al do not teach the preparation of a dilution of the target nucleic acid.

Brown et al teach the preparation of a dilution of the target nucleic acid (Abstract, Example 1, Table 1 and Figure 8);

Wittwer et al do not teach a method, wherein the amplified nucleic acids are detected with the aid of at least one fluorescent-labelled hybridization probe selected from TaqMan probes.

Brown et al teach a method, wherein the amplified nucleic acids are detected with the aid of at least one fluorescent-labelled hybridization probe selected from TaqMan probes (Column 3, lines 25-59).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the preparation of a dilution of the target nucleic acid and fluorescent-labelled hybridization probe selected from TaqMan probes of Brown et al in the method of sampling, amplifying and quantifying segment of nucleic acid of Wittwer et al. since Brown et al state, "A need also exists for performing multiple different amplification and detection reactions in parallel on a single specimen and for economizing usage of reagents in the process (Column 4, lines 23-26)". Moreover, Wittwer et al. state, "Monitoring the fluorescence of dsDNA once per cycle with dyes is an important advance that allows a wide dynamic range of initial template concentrations to be analyzed. However, the present invention's continuous monitoring within temperature cycles allows verification of product purity, simultaneous relative quantification with a competitor, and absolute product concentration determination (Page 66, lines 16-23)". An ordinary practitioner would have been motivated to

substitute and combine the preparation of a dilution of the target nucleic acid and fluorescent-labelled hybridization probe selected from TaqMan probes of Brown et al in the method of sampling, amplifying and quantifying segment of nucleic acid of Wittwer et al. in order to achieve the express advantages , as noted by Wittwer et al., of a method that allows a wide dynamic range of initial template concentrations to be analyzed and also allows verification of product purity, simultaneous relative quantification with a competitor, and absolute product concentration determination and also to achieve the express advantages , as noted by Brown et al., of a method for performing multiple different amplification and detection reactions in parallel on a single specimen and for economizing usage of reagents in the process .

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note

that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun kr. Chakrabarti

Arun Chakrabarti

Patent Examiner

Art Unit 1655

October 22, 2001